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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,530	03/17/2004	Jonathan Bingham	37087-8005.US01	3519
79975	7590	10/01/2008		
King & Spalding LLP P.O. Box 889 Belmont, CA 94002-0889			EXAMINER RIGGS II, LARRY D	
			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/802,530	Applicant(s) BINGHAM ET AL.	
	Examiner LARRY D. RIGGS II	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12 September 2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request for Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 18 July 2008 has been entered.

Status of Claims

Claims 15-21 are currently pending and under consideration.

Withdrawn Rejections/Objections

The objection of the abstract in the Office action mailed 29 January 2008 is withdrawn in view of the amendments filed 23 April 2008.

The rejection of claims 15-21 under 35 U.S.C. 112, Second Paragraph in the Office action mailed 29 January 2008 is withdrawn in view of the amendments filed 23 April 2008.

The rejection of claims 1-20 under 35 U.S.C. 102(e) over Loraine et al., in the Office action mailed 29 January 2008 is withdrawn in view of the amendments filed 23 April 2008.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn a method in a computer system for displaying a graphical representation of expression levels of a plurality of splice variants of a gene in one or more samples, each of the plurality of splice variants of the gene having modules the method comprising:

identifying modules for each splice variant of the gene, each module representing a subsequence of the splice variant selected from an exon and an intron and having a length,

applying a first mathematical function to the length of a first subsequence to obtain a scaled length for the first subsequence for graphical representation,

applying a second, different, mathematical function to the length of a second subsequence to obtain a scaled length for the second subsequence for graphical representation,

determining a relative expression level for each module by applying a mathematical algorithm to expression level data obtained using exon-exon junction indicator polynucleotides that selectively hybridize to exon-exon junctions of a given splice variant, and

displaying a graphical representation wherein the modules of the given splice variants are aligned with corresponding modules or exons of other splice variants of the gene, and wherein the representation indicates the relative expression levels of the modules and wherein the scaled length of the first subsequence and the scaled length of the second subsequence are displayed simultaneously.

Since the claimed invention involves mathematical algorithm, which is a judicial exception, the following analysis of facts of this particular patent application follows the rationale suggested in MPEP 2106.IV.C.2.

In the instant method claims 15-21, there is no physical transformation by the claimed invention because identifying modules, applying mathematical functions, determining a relative expression level and displaying a graphical representation are not physical transformations.

Since the claimed invention, claims 15-21, are a method, the following analysis of facts of this particular patent application follows the rationale suggested in Office's guidance to examiners under the Memorandum "Clarification of 'processes' under 35

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USC § 101", published May 15, 2008, available online

www.uspto.gov/web/patents/memorandum.htm

Paragraph three:

"Based on Supreme Court precedent¹ and recent Federal Circuit decisions, the Office's guidance to examiners is that a § 101 process must (1) be tied to another statutory class (such as a particular apparatus) or (2) transform underlying subject matter (such as an article or materials) to a different state or thing.² If neither of these requirements is met by the claim, the method is not a patent eligible process under §101 and should be rejected as being directed to nonstatutory subject matter."

The instant method claims 15-21 are not tied to another statutory class (such as a particular apparatus) either explicitly or inherently. Nominal or token recitations will not suffice, E.g. displaying, inputting, obtaining, etc. See *ex parte Langemyr*; Appeal 2008-1495, decided May 28, 2008. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites the limitation "displaying a graphical representation wherein the modules of the given splice variants are aligned with corresponding modules or exons of other splice variants of the gene" in lines 18-20. The metes and bounds of the

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limitation are unclear as to what the limitations "the given splice variants" and "other splice variants of the gene" pertains. The instant claim provides modules for each splice variant of the gene, wherein each module represents a subsequence, then the claim further provides a first subsequence (i.e. first module) scaled by a first function and second subsequence (i.e. second module) scaled by a second function. It is unclear whether the first subsequence and second subsequence are "the given splice variants".

Claim 15 recites the limitation "modules...are aligned with corresponding modules or exons of other splice variants". The metes and bounds of the limitation are unclear. The specification provides that a module is a subsequence of a gene product, (see specification, paragraph 37), and that some embodiments of the invention may contain both intronic and exonic modules, (see specification, paragraph 38 and Figures 1-5). In most examples provided by applicant, modules represent an intron or an exon, (see Figures 1-5). One skilled in the art would be unclear as to aligning modules and exons of said limitation, when examples in the specification have modules representing introns, exons and extension of exons and introns.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loraine et al. (US 2004/0049354).

The claims are drawn a method in a computer system for displaying a graphical representation of expression levels of a plurality of splice variants of a gene in one or more samples, each of the plurality of splice variants of the gene having modules the method comprising:

identifying modules for each splice variant of the gene, each module representing a subsequence of the splice variant selected from an exon and an intron and having a length,

applying a first mathematical function to the length of a first subsequence to obtain a scaled length for the first subsequence for graphical representation,

applying a second, different, mathematical function to the length of a second subsequence to obtain a scaled length for the second subsequence for graphical representation,

determining a relative expression level for each module by applying a mathematical algorithm to expression level data obtained using exon-exon junction indicator polynucleotides that selectively hybridize to exon-exon junctions of a given splice variant, and

displaying a graphical representation wherein the modules of the given splice variants are aligned with corresponding modules or exons of other splice variants of the gene, and wherein the representation indicates the relative expression levels of the modules and wherein the scaled length of the first subsequence and the scaled length of the second subsequence are displayed simultaneously.

Regarding claim 15, Loraine et al. shows modules, (e.g. Figure 3 of applicant's disclosure) of multiple splice variants with various lengths, (see paragraph 139; Figure 12); scaling the length of the modules of splice variants with a variety of scales that may vary in units and magnitude including linear, logarithmic and other types of scales, (see paragraph 137); applying a hybridization data to a model-fitting algorithm, wherein data

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may be obtained from exon-exon junction probes, i.e. data obtained from hybridizing exon-exon junction probes to splice variants, (see paragraphs 88, 89 and 113); and displaying a graphical representation of modules and exons of splice variants, wherein the representation indicates relative expression levels of the modules and exons (see paragraphs 5, 140, 141 and 144; Figure 12). While Loraine et al. shows different mathematical scaling to lengths of the modules of splice variants, (paragraph 137), Loraine only displays subsequences simultaneously in one scale. However, it would have been obvious for one having ordinary skill in the art to display simultaneously, two subsequences that had two different mathematical functions applied to the subsequences because Loraine et al. shows "it will be understood that many other graphical arrangements or devices known to those skill in the art may be used to distinguish splice variants and/or distinguish exons belonging to one or more splice variants", (paragraph 137).

Regarding claim 16, Loraine et al. shows non-overlapping exons and modules (see paragraph 144; Figure 12, 1210).

Regarding claim 17, the specification in paragraph 38, provides that the invention may display trimmed or extended exon in one module, while the remainder of the exon is another module. This is interpreted to mean that a partial exon may be displayed. Loraine et al. shows displaying modules of exons, introns or partial exons, (see paragraph 144).

Regarding claim 18, Loraine et al. shows exons and modules are constitutive, (See Figure 12, top two splice variants of 1210).

Regarding claim 19, Loraine et al. shows exons and modules are non-constitutive, (See Figure 12, comparing top two splice variants of 1210 with third splice variant of 1210, also referred in the figure 12 as 1211, selected splice variant).

Regarding claims 20 and 21, Loraine et al. shows scaling the length of the modules and exons of splice variants with a variety of scales that may vary in units and magnitude including linear, logarithmic and other types of scales, (see paragraph 137). This is interpreted to mean that to change scales by linear units or logarithmically, means to apply a linear or logarithmic function to the measured units of the current scale, respectively, (see paragraphs 137-138; Figure 12).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shubo (Joe) Zhou/
Primary Examiner, Art Unit 1631

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631